Remarks

Reconsideration of the application is respectfully requested in view of the foregoing amendments and following remarks. Claims 1, 2, 4-9 and 11 were pending. Claim 2 is canceled herein. Therefore, claims 1, 4-9, and 11 are pending, with claims 5-9 and 11 withdrawn. Consideration and allowance of the pending claims is requested.

Claims 1 and 4-6 are amended herein. Support for the claim amendments can be found throughout the specification, for example at page 4, lines 10-16; page 9, line 23-page 10, line 4; Example 2 (pages 25-27).

35 U.S.C. § 112, first paragraph

Claims 1, 2, and 4 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Claim 2 is canceled, making rejection of this claim moot. Claims 1 and 4-6 are amended herein to read on "an inhibitor of an α 1B subunit of N-type calcium channel."

The Office action alleges that the results of the behavioral tests performed on mice lacking expression of the α 1B subunit of the N-type calcium channel do not support a conclusion that this gene is directly involved in human depressive disorders. The Office action furthers asserts that it would require undue experimentation to extrapolate the results of the behavioral tests in knockout mice to methods of treatment of depression in view of the alleged lack of predictability of such extrapolation in the art or the instant specification. Applicants respectfully traverse, and request reconsideration.

Mice which lack expression of targets for anti-depressant drugs have been shown in the art to exhibit reduced immobility times in the tail suspension and forced swimming (behavioral despair) tests. For example, mice lacking expression of the norepinephrine transporter, a known target of anti-depressant drugs, had reduced immobility times compared to wild type mice in the Porsolt forced swim test and the tail suspension test (Xu *et al. Nat. Neurosci.* 3:465-471, 2000; *see* page 466, last paragraph and Fig. 3 a and b; herein submitted as **Exhibit A**). Similarly, mice lacking expression of the 5-HT1A receptor demonstrated reduced immobility in the forced swim test (Ramboz *et al. Proc. Natl. Acad. Sci. USA* 95:14476-14481, 1998; see page 14479, last paragraph and Figure 5; herein submitted as

Exhibit B). 5-HT1A receptor antagonists have been shown to induce faster onset and to increase efficacy of anti-depressant treatment (see *e.g.* U.S. Pat. No. 6,312,717). Further, mice lacking expression of the neurokinin 1 receptor (NK1R) showed increased struggle (decreased immobility) in the tail suspension test, and their behavior in the forced swim test resembled wild type mice treated with the antidepressant drug fluoxetine (Rupniak, *et al. Behav. Pharmacol.* 12:497-508, 2001; herein submitted as **Exhibit C**). NK1R antagonists have been described for treatment of major depressive disorder (see *e.g.* U.S. Patent Nos. 6,613,765 and 7,235,541). Based on the foregoing, the state of the art indicates that knockout of targets of known anti-depressant drugs reduces immobility in the tail suspension and forced swim behavioral tests. Therefore, one of skill in the art would be able to extrapolate that inhibitors of the gene knocked out in a mouse exhibiting reduced immobility in these behavioral tests would be useful in a method for treating depression.

Therefore, the specification is fully enabled for the scope of the claims, and Applicants request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

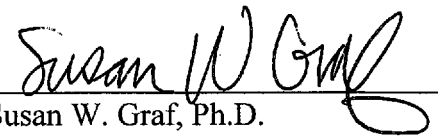
Conclusion

As the present amendment places the application in condition for allowance, Applicants request that it be entered. If any matters remain to be discussed before a Notice of Allowance is issued, the Examiner is respectfully requested to contact the undersigned for a telephone interview at the telephone number listed below.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 595-5300
Facsimile: (503) 595-5301

By 
Susan W. Graf, Ph.D.
Registration No. 60,432